

Serial No.: 10/661,977

IN THE CLAIMS:

Please amend the claims as follows:

1-7. (Canceled)

8. (Currently amended) An *in vivo* method of monitoring the localization and distribution of a compound of interest to a desired site in an organism by magnetic resonance imaging, the method comprising:

- (a) administering an envirosensitive liposome composition to a subject, the composition comprising:
 - (i) a contrast agent;
 - (ii) a compound of interest; and
 - (iii) an envirosensitive liposome encapsulating the contrast agent and the compound of interest; and
- (b) monitoring the localization and distribution of the compound of interest to a desired site by magnetic resonance imaging, wherein the monitoring comprises monitoring release of the contents of the liposome by monitoring an increase in the presence of contrast agent as the contents of the liposome are being released.

9. (Previously presented) The method of claim 8, further comprising increasing blood flow to the desired site.

10. (Previously presented) The method of claim 9, wherein the increasing blood flow comprises heating the desired site.

11. (Currently amended) The method of claim 10, wherein the increasing blood flow is by a method selected from the group consisting of contacting a heated

Serial No.: 10/661,977

catheter with the desired site, applying RF or microwave energy to the site, applying ultrasonic energy to the site and applying a laser beam to the site.

12. (Previously presented) The method of claim 8, wherein the envirosensitive liposome is a liposome selected from the group consisting of a thermosensitive liposome, a pH-sensitive liposome, a chemosensitive liposome and a radiation-sensitive liposome.

13. (Previously presented) The method of claim 8, wherein the desired site is a tumor.

14. (Previously presented) The method of claim 12, wherein the thermosensitive liposome comprises a formulation selected from the group consisting of DPPC-PEG₂₀₀₀, DPPC-DSPE-PEG₂₀₀₀ (95:5, mol:mol); DPPC-MSPC-DSPE-PEG₂₀₀₀ (90:10:4, mol:mol).

15. (Previously presented) The method of claim 8, wherein the contrast agent comprises a element selected from the group consisting of Gd, Cu, Cr, Fe, Co, Er, Ni, Eu, Dy, Zn, Mg, Mo, Li, Ta, and Mn.

16. (Previously presented) The method of claim 8, wherein the compound of interest is a chemotherapeutic agent.

17. (Previously presented) The method of claim 8, further comprising exposing the envirosensitive liposome at the desired site to a non-physiological environmental condition.

Serial No.: 10/661,977

18. (Previously presented) The method of claim 17, wherein the environmental condition is selected from the group consisting of hyperthermia, electromagnetic radiation, a chemical agent and non-physiological pH.

19. (Currently amended) A method of detecting an *in vivo* blood pool, the method comprising:

- (a) administering a liposome composition to a subject, the composition comprising:
 - (i) a contrast agent; and
 - (ii) a liposome encapsulating the contrast agent, wherein the liposome composition has the ability to remain in the subject's blood stream for a protracted period of time without being recognized by the subject's reticuloendothelial system;
- (b) generating a magnetic resonance image of a site of interest; and
- (c) detecting the presence of an *in vivo* blood pool by analyzing the magnetic resonance image.

20. (Previously presented) The method of claim 19, wherein the liposome composition comprises a non-sensitive liposome composition.

21. (Previously presented) The method of claim 20, wherein the non-sensitive liposome comprises DSPC/Cholesterol (55:45, mol:mol).

22. (Previously presented) The method of claim 19, wherein the liposome composition comprises an envirosensitive liposome composition.

23. (Previously presented) The method of claim 22, wherein the envirosensitive liposome composition is selected from the group consisting of a

Serial No.: 10/661,977

thermosensitive liposome composition, a pH-sensitive liposome composition, a chemosensitive liposome and a radiation-sensitive liposome composition.

24. (Previously presented) The method of claim 23, wherein the thermosensitive liposome composition comprises a formulation selected from the group consisting of DPPC-PEG₂₀₀₀, DPPC-DSPE-PEG₂₀₀₀ (95:5, mol:mol); DPPC-MSPC-DSPE-PEG₂₀₀₀ (90:10:4, mol:mol).

25. (Previously presented) The method of claim 22, wherein the contrast agent comprises a element selected from the group consisting of Gd, Cu, Cr, Fe, Co, Er, Ni, Eu, Dy, Zn, Mg, Mo, Li, Ta, and Mn.

26. (Previously presented) The method of claim 19, wherein the site of interest comprises a structure selected from the group consisting of a tumor, an embolism, an ischemia, an injury site, and a tissue edema.

27. (Previously presented) The method of claim 19, wherein the analyzing comprises examining the image to detect the presence of an accumulation of contrast agent, wherein an accumulation of contrast agent indicates the presence of a blood pool.

28. (Previously presented) The method of claim 27, wherein the examining comprises making a pixel density determination.

29. (Currently amended) A method of monitoring the accumulation of a compound of interest at a desired site *in vivo* by magnetic resonance imaging, the method comprising:

- (a) administering to a subject an envirosensitive liposome composition comprising:

Serial No.: 10/661,977

- (i) a contrast agent;
 - (ii) a compound of interest; and
 - (iii) an envirosensitive liposome encapsulating the contrast agent and the compound of interest; and
- (b) monitoring the accumulation of the compound of interest at a desired site by magnetic resonance imaging, wherein the monitoring comprises tracking the release of the contents of the liposome by monitoring an increase in the presence of contrast agent.

30. (Previously presented) The method of claim 29, wherein the site of interest is selected from the group consisting of a tumor, injury site, and tissue edema.

31. (Previously presented) The method of claim 29, wherein the envirosensitive liposome is a liposome selected from the group consisting of a thermosensitive liposome, a pH-sensitive liposome, a chemosensitive liposome and a radiation-sensitive liposome.

32. (Previously presented) The method of claim 31, wherein the thermosensitive liposome comprises a formulation selected from the group consisting of DPPC-PEG₂₀₀₀, DPPC-DSPE-PEG₂₀₀₀ (95:5, mol:mol); DPPC-MSPC-DSPE-PEG₂₀₀₀ (90:10:4, mol:mol)

33. (Previously presented) The method of claim 29, wherein the contrast agent comprises a element selected from the group consisting of Gd, Cu, Cr, Fe, Co, Er, Ni, Eu, Dy, Zn, Mg, Mo, Li, Ta, and Mn.

34. (Previously presented) The method of claim 29, wherein the compound of interest is a chemotherapeutic agent.

Serial No.: 10/661,977

35. (Canceled)

36. (Currently amended) The method of claim ~~[[35]]~~ 45, wherein the thermosensitive liposome comprises a formulation selected from the group consisting of DPPC-PEG₂₀₀₀, DPPC-DSPE-PEG₂₀₀₀ (95:5, mol:mol); DPPC-MSPC-DSPE-PEG₂₀₀₀ (90:10:4, mol:mol)

37. (Currently amended) The method of claim ~~[[35]]~~ 45, wherein the contrast agent is selected from the group consisting of Gd, Cu, Cr, Fe, Co, Er, Ni, Eu, Dy, Zn, Mg, Mo, Li, Ta, and Mn.

38. (Currently amended) The method of claim ~~[[35]]~~ 45, wherein the heating is by a method selected from the group consisting of contacting a heated material with the site of interest, applying RF or microwave energy to the site, applying ultrasonic energy to the site and applying a laser beam to the site.

39. (Currently amended) The method of claim ~~[[35]]~~ 45, wherein steps (a)-(c) are repeated a desired number of times.

40. (Previously presented) The method of claim 39, wherein two or more thermosensitive liposomes are employed, each having a different T_m .

41. (Canceled)

42. (Currently amended) An *in vivo* method of monitoring the localization and distribution of a compound of interest to a desired site in an organism by magnetic resonance imaging, the method comprising:

Serial No.: 10/661,977

- (a) administering an envirosensitive liposome composition to a subject, the composition comprising:
 - (i) a contrast agent;
 - (ii) a compound of interest; and
 - (iii) an envirosensitive liposome encapsulating the contrast agent and the compound of interest; and
- (b) monitoring in real time the localization and distribution of the compound of interest to a desired site by magnetic resonance imaging, wherein the monitoring comprises monitoring release of the contents of the liposome by monitoring an increase in the presence of contrast agent as the contents of the liposome are being released.

43. (Currently amended) A method of detecting an *in vivo* blood pool, the method comprising:

- (a) administering a liposome composition to a subject, the composition comprising:
 - (i) a contrast agent; and
 - (ii) a liposome encapsulating the contrast agent, wherein the liposome composition has the ability to remain in the subject's blood stream for a protracted period of time without being recognized by the subject's reticuloendothelial system;
- (b) generating a magnetic resonance image of a site of interest; and
- (c) detecting in real time the presence of an *in vivo* blood pool by analyzing the magnetic resonance image.

44. (Currently amended) A method of monitoring the accumulation of a compound of interest at a desired site *in vivo* by magnetic resonance imaging, the method comprising:

Serial No.: 10/661,977

- (a) administering to a subject an envirosensitive liposome composition comprising:
 - (i) a contrast agent;
 - (ii) a compound of interest; and
 - (iii) an envirosensitive liposome encapsulating the contrast agent and the compound of interest; and
- (b) monitoring in real time the accumulation of the compound of interest at a desired site by magnetic resonance imaging, wherein the monitoring comprises monitoring release of the contents of the liposome by monitoring an increase in the presence of contrast agent as the contents of the liposome are being released.

45. (Previously presented) A method of generating a heating profile of a site of interest, the method comprising:

- (a) administering to a subject a thermosensitive liposome composition comprising:
 - (i) a contrast agent; and
 - (ii) a thermosensitive liposome encapsulating the contrast agent and the compound of interest and having a melting temperature T_m ;
- (b) heating a site of interest in a subject;
- (c) monitoring release of the contrast agent from the thermosensitive liposome using magnetic resonance imaging; and
- (d) generating in real time a heating profile of the site of interest, wherein heating of an area to a temperature of at least T_m is indicated by release of contrast agent.

Serial No.: 10/661,977

46. (Previously presented) The method of claim 29, wherein there is increased blood flow to the desired site.

Please add the following new claim:

47. (New) The method of claim 19, wherein the blood pool is indicative of a vascular irregularity.